CLAIMS

1. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula X_1-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-X_2 wherein

X_1 is from zero to twelve amino acids, and
X_2 is from zero to twelve amino acids,

and wherein said compound optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

2. The composition of claim 1 wherein

X_1 is from zero to six amino acids, and
X_2 is from zero to six amino acids.

3. The composition of claim 1 wherein

X_1 is

(i) zero amino acids, or

(ii) the segment Thr-Leu-Thr-His-Thr–Ile-Thr-Lys-Leu-Asn-Ala-Glu, or N-terminal truncation fragment thereof containing at least one amino acid, and

X_2 is

(i) zero amino acids, or

(ii) the segment Ile-Asp-Asn-Val-Lys-Lys-Ala-Arg-Val-Gln-Val-Val, or C-terminal truncation fragment thereof containing at least one amino acid.

4. The composition of claim 1 wherein the compound has

substantial amino acid sequence homology to the amino acid sequence Thr-Leu-Thr-His-Thr-Ile-Thr-Lys-Leu-Asn-Ala-Glu-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-Ile-Asp-Asn-Val-Lys-Lys-Ala-Arg-Val-Gln-Val-Val.

5. The composition of claim 1 wherein the compound has the amino acid sequence Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys.

6. The composition of claim 1 wherein the compound has the amino acid sequence Thr-Ile-Thr-Lys-Leu-Asn-Ala-Glu-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys.

7. The composition of claim 1 wherein the compound has the amino acid sequence Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-Ile-Asp-Asn-Val-Lys-Lys-Ala-Arg.

8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula X_3-Cys-Val-Gly-Cys-X_4 wherein

X_3 is from zero to twelve amino acids, and

X_4 is from zero to twelve amino acids,

wherein a disulfide bond between the cysteine residues of the segment Cys-Val-Gly-Cys is optionally present, and wherein said compound optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

9. The composition of claim 8 wherein

X_3 is from zero to six amino acids, and

X_4 is from zero to six amino acids.

10. The composition of claim 8 wherein

X_3 is

(i) zero amino acids, or

(ii) the segment Gly-Lys-Asp-Phe-Val-Gln-Pro-Pro-Thr-Lys-Ile, or N-terminal truncation fragment thereof containing at least one amino acid, and

X_4 is

(i) zero amino acids, or

(ii) the segment Pro-Arg-Asp-Ile-Pro-Thr-Asn-Ser-Pro-Glu-Leu-Glu, or C-terminal truncation fragment thereof containing at least one amino acid.

11. The composition of claim 8 wherein the compound has substantial amino acid sequence homology to the amino acid sequence Pro-Gln-Lys-Asp-Phe-Val-Gln-Pro-Pro-Thr-Lys-Ile-Cys-Val-Gly-Cys-Pro-Arg-Asp-Ile-Pro-Thr-Asn-Ser-Pro-Glu-Leu-Glu

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12. The composition of claim 8 wherein the compound has the amino acid sequence Cys-Val-Gly-Cys.

13. The composition of claim 8 wherein the compound has the amino acid sequence Thr-Lys-Ile-Cys-Val-Gly-Cys-Pro-Arg-Asp-Ile-Pro-Thr-Asn-Ser-Pro.

14. The composition of any of claims 8-13 wherein a disulfide bond between the cysteine residues of the segment Cys-Val-Gly-Cys of said compound is present.

15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound of the formula X_5-Leu-Asp-X_7-Asn-Ala-Glu-Val-Tyr-X_6 wherein

X_5 is from zero to twelve amino acids,

X_6 is from zero to twelve amino acids, and

X_7 is Ala or Cys,

and wherein said compound optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

16. The composition of claim 15 wherein

X_5 is from zero to six amino acids, and

X_6 is from zero to six amino acids.

17. The composition of claim 15 wherein

X_5 is

(i) zero amino acids, or

(ii) the segment Thr-Glu-Ser-Cys-Glu-Thr-Lys-Lys-Leu-Gly-Gln-Ser, or N-terminal truncation fragment thereof containing at least one amino acid, and

X_6 is

(i) zero amino acids, or

(ii) the segment Val-Val-Pro-Trp-Glu-Lys-Lys-Ile-Tyr-Pro-Thr-Val, or C-terminal truncation fragment thereof containing at least one amino acid.

18. The composition of claim 15 wherein the compound has substantial amino acid sequence homology to the amino acid sequence Thr-Glu-Ser-Cys-Glu-Thr-Lys-Lys-Leu-Gly-Gln-Ser-Leu-Asp-Ala-Asn-Ala-Glu-Val-Tyr-Val-Val-Pro-Trp-Glu-Lys-Lys-Ile-Tyr-Pro-Thr-Val.

19. The composition of claim 15 wherein the compound has the amino acid sequence Leu-Asp-Ala-Asn-Ala-Glu-Val-Tyr.

20. The composition of claim 15 wherein the compound has the amino acid sequence Glu-Thr-Lys-Lys-Leu-Gly-Gln-Ser-Leu-Asp-Ala-Asn-Ala-Glu-Val-Tyr.

21. The composition of claim 15 wherein the compound has the amino acid sequence Leu-Asp-Ala-Asn-Ala-Glu-Val-Tyr-Val-Val-Pro-Trp-Glu-Lys-Lys-Ile.

22. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a peptide fragment of high molecular weight kininogen domain 3, or analog of such a peptide fragment wherein one or more cysteine residues in the fragment are replaced by alanine residues, which peptide fragment or analog inhibits endothelial cell proliferation and optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

23. The composition according to claim 22 wherein the peptide fragment or analog has the amino acid sequence Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-Cys-Ser-Lys-Glu-Ser or Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-Ala-Ser-Lys-Glu-Ser.

24. A method of inhibiting angiogenesis comprising administering to a mammal an effective amount of a composition according to claim 1.

25. A method of inhibiting endothelial cell proliferation comprising administering to a mammal an effective amount of a composition according to claim 1.

26. A method of inducing endothelial cell apoptosis comprising administering to a mammal an effective amount of a compound according to claim 1.

27. A method of inhibiting endothelial cell proliferation comprising contacting endothelial cells with a compound of the formula X_1-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-X_2 wherein

X_1 is from zero to twelve amino acids, and
X_2 is from zero to twelve amino acids,

and wherein said compound optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

28. The method of claim 27 wherein

X_1 is from zero to six amino acids, and
X_2 is from zero to six amino acids.

29. The method of claim 27 wherein

X_1 is

(i) zero amino acids, or

(ii) the segment Thr-Leu-Thr-His-Thr–Ile-Thr-Lys-Leu-Asn-Ala-Glu, or N-terminal truncation fragment thereof containing at least one amino acid, and

X_2 is

(i) zero amino acids, or

(ii) the segment Ile-Asp-Asn-Val-Lys-Lys-Ala-Arg-Val-Gln-Val-Val, or C-terminal truncation fragment thereof containing at least one amino acid.

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30. The method of claim 27 wherein the compound has the amino acid sequence Thr–Ile-Thr-Lys-Leu-Asn-Ala-Glu-Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys.

31. The method of claim 27 wherein the compound has the amino acid sequence Asn-Asn-Ala-Thr-Phe-Tyr-Phe-Lys-Ile-Asp-Asn-Val-Lys-Lys-Ala-Arg.

32. A method of inhibiting endothelial cell proliferation comprising contacting endothelial cells with a compound of the formula X_3-Cys-Val-Gly-Cys-X_4 wherein

X_3 is from zero to twelve amino acids, and

X_4 is from zero to twelve amino acids,

wherein a disulfide bond between the cysteine residues of the segment Cys-Val-Gly-Cys is optionally present, and wherein said compound optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

33. The method of claim 32 wherein

X_1 is from zero to six amino acids, and
X_2 is from zero to six amino acids.

34. The method of claim 32 wherein

X_3 is

(i) zero amino acids, or

(ii) the segment Gly-Lys-Asp-Phe-Val-Gln-Pro-Pro-Thr-Lys-Ile, or N-terminal truncation fragment thereof containing at least one amino acid, and

X_4 is

(i) zero amino acids, or

(ii) the segment Pro-Arg-Asp-Ile-Pro-Thr-Asn-Ser-Pro-Glu-Leu-Glu, or C-terminal truncation fragment thereof containing at least one amino acid.

35. The method of claim 32 wherein the compound has the amino acid sequence Cys-Val-Gly-Cys.

36. The method of claim 32 wherein the compound has the amino acid sequence Thr-Lys-Ile-Cys-Val-Gly-Cys-Pro-Arg-Asp-Ile-Pro-Thr-Asn-Ser-Pro.

37. The method of any of claims 32-36 wherein a disulfide bond between the cysteine residues of the segment Cys-Val-Gly-Cys of said compound is present.

38. A method of inhibiting endothelial cell proliferation comprising

contacting endothelial cells with a compound of the formula X_5-Leu-Asp-X_7-Asn-Ala-Glu-Val-Tyr-X_6 wherein

X_5 is from zero to twelve amino acids,
X_6 is from zero to twelve amino acids, and
X_7 is Ala or Cys.

and wherein said compound optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

39. The method of claim 38 wherein

X_5 is from zero to six amino acids, and
X_6 is from zero to six amino acids.

40. The method of claim 38 wherein

X_5 is

(i) zero amino acids, or

(ii) the segment Thr-Glu-Ser-Cys-Glu-Thr-Lys-Lys-Leu-Gly-Gln-Ser, or N-terminal truncation fragment thereof containing at least one amino acid, and

X_6 is

(i) zero amino acids, or

(ii) the segment Val-Val-Pro-Trp-Glu-Lys-Lys-Ile-Tyr-Pro-Thr-Val, or C-terminal truncation fragment thereof containing at least one amino acid.

41. The method of claim 38 wherein the compound has the amino acid sequence Leu-Asp-Ala-Asn-Ala-Glu-Val-Tyr.

42. The method of claim 38 wherein the compound has the amino acid sequence Glu-Thr-Lys-Lys-Leu-Gly-Gln-Ser-Leu-Asp-Ala-Asn-Ala-Glu-Val-Tyr.

43. The method of claim 38 wherein the compound has the amino acid sequence Leu-Asp-Ala-Asn-Ala-Glu-Val-Tyr-Val-Val-Pro-Trp-Glu-Lys-Lys-Ile.

44. A method of inhibiting endothelial cell proliferation comprising contacting endothelial cells with a peptide fragment of high molecular weight kininogen domain 3, or analog of such a peptide fragment wherein one or more cysteine residues in the fragment are replaced by alanine residues, wherein said compound optionally comprises an amino-terminal and/or carboxy-terminal protecting group.

45. The method according to claim 44 wherein the peptide has the amino acid sequence Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-Cys-Ser-Lys-Glu-Ser or Tyr-Phe-Ile-Asp-Phe-Val-Ala-Arg-Glu-Thr-Thr-Ala-Ser-Lys-Glu-Ser.